Intra-annular vs. supra-annular Valve Considerations

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Potential Conflicts of Interest

Speaker's name: Prof. Axel Linke

I have the following potential conflicts of interest to declare:

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>• Grant/Research Support</td>
<td>• Novartis</td>
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<td>• Consulting Fees/Honoraria</td>
<td>• Medtronic, Abbott, Edwards Lifesciences,</td>
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<td>Boston Scientific, Astra Zeneca, Novartis,</td>
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<td>Pfizer, Abiomed, Bayer, Boehringer</td>
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<tr>
<td>• Major Stock Shareholder/Equity</td>
<td>• Claret Medical Inc., Picardia, Transverse</td>
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<td>• Royalty Income</td>
<td>Medical</td>
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<tr>
<td>• Ownership/Founder</td>
<td>• None</td>
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<td>• Intellectual Property Rights</td>
<td>• None</td>
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<td>• Other Financial Benefit</td>
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<table>
<thead>
<tr>
<th>Patient-specific consideration</th>
<th>Center-specific consideration</th>
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<tbody>
<tr>
<td>- valve type (tric. vs. bic.)</td>
<td>- local practice</td>
</tr>
<tr>
<td>- calcification</td>
<td>- operator training</td>
</tr>
<tr>
<td>- coronary disease</td>
<td>- medical center experience</td>
</tr>
<tr>
<td>- anatomy of the aorta</td>
<td>- availability</td>
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</table>
Valve Type Selection - Choices

- self-expandable intra-annular
- self-expandable supra-annular
- balloon-expandable intra-annular
- actively-expandable sub-annular
Why is this important

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**self-expandable**
- **intra-annular**
  - maybe higher gradients, because the valve functions where the calcified leaflet are

**self-expandable**
- **supra-annular**
  - maybe lower gradients, because the valve functions above the calcified leaflet

**ballon-expandable**
- **intra-annular**
  - maybe higher gradients, because the valve functions where the calcified leaflet are

**actively-expandable**
- **sub-annular**
  - maybe higher gradients, because the LVOT is smaller than the annulus
Why is this important

**self-expandable**

- intra-annular
  - good coronary access
  - redo possible, no restrictions of coronaries

**self-expandable**

- supra-annular
  - coronary access impaired
  - redo possible, no coronary access afterwards

**ballon-expandable**

- intra-annular
  - good coronary access
  - redo possible, no restrictions of coronaries

**actively-expandable**

- sub-annular
  - coronary access ok
  - redo possible, no restrictions of coronaries
- **Low profile** delivery system

- **Flexible and deliverable** system tracks through tortuous, complex anatomy

- **Early valve functionality** for hemodynamic stability throughout deployment

- **No rapid pacing** required

- **Large open cells** minimize obstruction to coronary blood flow and preserve coronary access

- **Nitinol self-expanding stent** is fully recapturable, repositionable and retrievable

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<table>
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<tr>
<th>Patient Annulus (mm)</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
<th>24</th>
<th>25</th>
<th>26</th>
<th>27</th>
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<tbody>
<tr>
<td>Valve Size (mm)</td>
<td>23</td>
<td>25</td>
<td>27</td>
<td></td>
<td></td>
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*Until fully deployed.
2. Portico IFU.

Information contained herein for DISTRIBUTION outside of the U.S. ONLY. Check the regulatory status of the device in areas where CE marking is not the regulation in force.
**Pivotal RCT**
Enrollment began May 2014

**Pivotal RCT**
Enrollment complete Oct 2017

**FlexNav DS Cohort**
Enrollment Nov 2018- Jun 2019

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**PMA Submission**

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<td><strong>Pause</strong></td>
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2014 - 2019

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Portico IDE Trial Design
750 randomized subjects enrolled from 52 sites in US and AUS between May 2014 to Oct 2017

**750 Randomized (ITT)**

- **381 Assigned Portico valve**
  - 375 Treatment Initiated
    - 371 Implanted
      - 30 Day FU: 97.5%
      - 1 Year FU: 97.4%
  - 3 Did not meet eligibility criteria
  - 2 Withdrew informed consent
  - 1 Investigator decision
  - 2 Died during implant procedure
  - 1 Unable to gain vascular access

- **369 Assigned Commercial valve**
  - 362 Treatment Initiated
    - 361 Implanted
      - 30 Day FU: 97.2%
      - 1 Year FU: 98.1%
  - 3 Withdrew informed consent
  - 2 Died before procedure
  - 1 Did not meet eligibility criteria
  - 1 Randomized after subject expired
  - 1 Converted to SAVR
  - 1 Unable to gain vascular access

**ITT = Intention-to-Treat population**
Pivotal RCT: Hemodynamics

Mean Gradient

<table>
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<tr>
<th>Valve Type</th>
<th>Baseline</th>
<th>Discharge</th>
<th>30 Days</th>
<th>6 Months</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>Portico valve</td>
<td>44.3</td>
<td>1.8</td>
<td>1.7</td>
<td>1.7</td>
<td>1.8</td>
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<tr>
<td>Commercial valve</td>
<td>43.7</td>
<td>1.9</td>
<td>1.7</td>
<td>1.7</td>
<td>1.8</td>
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AVA

<table>
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<tr>
<th>Valve Type</th>
<th>Baseline</th>
<th>Discharge</th>
<th>30 Days</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portico valve</td>
<td>43.5</td>
<td>10.4</td>
<td>10.2</td>
<td>10.1</td>
<td>10.6</td>
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<tr>
<td>Commercial valve</td>
<td>42.0</td>
<td>9.0</td>
<td>8.4</td>
<td>8.5</td>
<td>8.6</td>
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</table>

Mean Aortic Gradient (mmHg) | Portico valve (n=381) | Commercial valve (n=369)

Baseline: 372 357
Discharge: 360 346
30 Days: 337 340
6 Months: 298 297
12 Months: 274 273

AVA (cm²)

Baseline: 349 341
Discharge: 327 326
30 Days: 321 317
6 Months: 276 279
12 Months: 252 262
Portico valve Vs. EDW

Portico valve Vs. MDT

Proprietary and confidential — do not distribute
• Moderate or greater PVL is higher in Portico valve group
• 63% of all commercial valves implanted had a PVL reducing feature
Patient- and center-specific factors will impact on valve type selection.

Patient factors, center and operator volume will impact on outcomes.

Self-expandable valves seem to have a better hemodynamic profile (lower gradients and higher valve orifice areas).
If the patient has significant CAD (with previous interventions or a high likelihood of future interventions) a THV should be selected that allows good coronary access.

If there is a likelihood that the patient will require a redo (young patients, dialysis etc.) the first THV should be one with an intraannular or subannular valve function.
Thank you